HIV and TB in the Rural Southeast

Beth Gadkowski

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TB and HIV in the Rural Southeast

L. Beth Gadkowski MD MPH MS
Clinical Associate Professor
Division of Infectious Diseases
University of Florida
Disclosure Information

I do not have any conflicts of interest to disclose and I do not intend to discuss off label use of any drug or treatment during this discussion.
Objectives

- Describe the global and local epidemiology of TB/HIV coinfection
- Utilize TSTs and IGRAs appropriately in the diagnosis of LTBI in people living with HIV (PLWH)
- Identify the signs and symptoms of active TB in PLWH
- Develop a treatment plan for an TB/HIV coinfected patient
Objectives

§ Describe the global and local epidemiology of TB/HIV coinfection

§ Utilize TSTs and IGRAs appropriately in the diagnosis of LTBI in people living with HIV (PLWH)

§ Identify the signs and symptoms of active TB in PLWH

§ Develop a treatment plan for an TB/HIV coinfected patient
TB Case Rates,* United States, 2016

*Cases per 100,000; as of June 21, 2017.
DC, District of Columbia; NYC, New York City (excluded from New York state)

Estimated HIV Coinfection Among Persons Reported with TB, United States, 1993–2016*

* As of June 21, 2017.

Note: Minimum estimates are based on reported HIV-positive status among all TB patients in the age group.

TB/HIV in Georgia, 2016

- 301 new TB cases (2.9 cases per 100000)
- 48% foreign-born persons
- 11% HIV positive
  - 80% non-Hispanic, Black
  - 73% male
  - 50% age 45-64

Figure 12. HIV Status of TB Cases, Georgia, 1996-2016
Figure 3. Number of TB Cases by Health Districts, Georgia, 2016

Number of TB Cases:
- Low incidence: 1-10
- Medium incidence: 11-18
- High incidence: >18 (29-58)

*HIV-positive by Health District:
1.1 Rome: 20% (5)
3.1 Cobb: 7% (29)
3.2 Fulton: 30% (44)
3.4 Lawrenceville: 11% (37)
3.5 DeKalb: 9% (58)
5.2 Macon: 11% (9)
6.0 Augusta: 17% (18)
7.0 Columbus: 6% (17)
HIV and Tuberculosis

- HIV increases the risk of TB reactivation enormously.
  - TST+, HIV- $\Rightarrow$ lifetime risk $\sim 10\%$
  - TST+, HIV+ $\Rightarrow$ YEARLY risk $\sim 10\%$
- A deadly duo

He lives with HIV
But tuberculosis nearly killed him
TB Risk Factors in HIV

Sociodemographic:
- Black, Asian or Hispanic ethnicity
- Birth or long-term residence in a country with high TB incidence
- HIV acquisition through IDU/active IDU use
- Homelessness
- Proximity to active TB case

Clinical:
- Low CD4 count
- High viral load
- Failure of (or late) initiation of ART

Winter et al. IJTLID (7):713-722 · July 2018
In addition to HIV...

- TB disproportionately affects vulnerable populations: recent immigrants, homeless, incarcerated or have problems with substance abuse
- These populations are “hard to reach” and are linked by poverty, social deprivation and difficulty in accessing health care
Barriers to Care

- **Stigma**: may prevent patients from accepting supervised treatment in their homes, where visits from health care workers would be immediately noticed by the community; fear of being laid off or fired if TB is discovered; loss of community due to isolation; reluctance to disclose contacts can lead to outbreaks

- **Lack of access to health care**: lack of insurance, lack of providers, distance to facility, no transportation, having to choose between work and care

- **Distrust of medical community**

- Delays in correct TB diagnosis and initiation of effective TB treatment increases TB morbidity/mortality, risk of transmission and development of drug-resistant TB
TB Prevention

- Early HIV diagnosis with early initiation of ART
- ART results in a prompt and marked decrease in the incidence of TB disease
- HIV-related TB incidence has declined more rapidly than the rate of active TB in the general population, in part due to the widespread use of ART
- Even with the beneficial effects of ART, the risk of TB disease among persons with HIV infection remains greater than that of the general population
TB Prevention--LTBI

- Treatment of latent TB infection (LTBI) (as defined by a positive tuberculin skin test [TST]) decreases the risk of TB disease by 62% and the risk of death by 26% among persons with HIV infection
- Prevention of TB disease by screening and appropriate treatment for LTBI are key components of HIV care
# Latent TB Infection vs. Active TB Disease

<table>
<thead>
<tr>
<th>Latent TB Infection</th>
<th>Active TB Disease</th>
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<tbody>
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</table>

### Can my Latent TB Infection (sleeping germs) wake up and make me sick with Active TB Disease?

Yes, and certain factors increase my risk!
- I arrived recently from another country where TB is common.
- I have HIV.
- I was in close contact with someone with active TB disease.
- I have diabetes, kidney failure, or cancer.
- I had surgery to remove part of my stomach.
- I live or work in a hospital, jail, drug rehab center or shelter.
- I use injection drugs.
- I have received an organ transplant.
- I take certain medications that affect my immune system, like prednisone (steroids) or other pills or injections to treat certain types of skin, joint and gastrointestinal conditions.

### If I have Latent TB Infection, can I reduce my chances of getting sick with Active TB Disease?

Yes, I can prevent tuberculosis!

I can take safe, effective medicines.

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Published 2012

[Logos of institutions: HHC, NYU School of Medicine, NYU Langone Medical Center, UF, Southeren National Tuberculosis Center]
When to Test for LTBI

- Test for LTBI at initiation of HIV care
- Repeat LTBI testing:
  - If initial test negative and subsequent CD4 cell count rises to >200 cells/mm$^3$
  after the initiation of antiretroviral therapy

Guidelines for Prevention and Treatment of Opportunistic Infections in HIV-Infected Adults and Adolescents
https://aidsinfo.nih.gov/guidelines
Repeat LTBI testing (if baseline test negative) **annually** if there is ongoing high risk for TB exposure:

- Current or history of incarceration
- Live in congregate settings
- Active drug abuse (IVDA, crack cocaine)
- Marginal housing or homelessness
- Travel to TB-endemic locations
Tuberculin Skin Testing

- Inject 0.1 ml of standardized mix of TB proteins (purified protein derivative)
- Given intradermally on volar forearm
- Measure induration 48-72 hrs after placement
- Measure in millimeters, not “positive” or “negative”
- Should be interpreted by well-trained health care professional

Picture from: www.info.gov.hk/dh/diseases/CD/TB.htm
Interpreting a Tuberculin Skin Test (TST)

<table>
<thead>
<tr>
<th>Classification of the Tuberculin Skin Test Reaction</th>
</tr>
</thead>
<tbody>
<tr>
<td>An induration of 5 or more millimeters is considered positive in:</td>
</tr>
<tr>
<td>• HIV-infected persons</td>
</tr>
<tr>
<td>• A recent contact of a person with TB disease</td>
</tr>
<tr>
<td>• Persons with fibrotic changes on chest radiograph consistent with prior TB</td>
</tr>
<tr>
<td>• Patients with organ transplants</td>
</tr>
<tr>
<td>• Persons who are immunosuppressed for other reasons (e.g., taking the equivalent of ≥15 mg/day of prednisone for 1 month or longer, taking TNF-alpha antagonists)</td>
</tr>
<tr>
<td>An induration of 10 or more millimeters is considered positive in:</td>
</tr>
<tr>
<td>• Recent immigrants (&lt; 5 years) from high-prevalence countries</td>
</tr>
<tr>
<td>• Injection drug users</td>
</tr>
<tr>
<td>• Residents and employees of high-risk congregate settings</td>
</tr>
<tr>
<td>• Mycobacteriology laboratory personnel</td>
</tr>
<tr>
<td>• Persons with clinical conditions that place them at high risk</td>
</tr>
<tr>
<td>• Children &lt; 4 years of age</td>
</tr>
<tr>
<td>• Infants, children, and adolescents exposed to adults in high-risk categories</td>
</tr>
</tbody>
</table>

An induration of 15 or more millimeters is considered positive in any person, including persons with no known risk factors for TB. However, targeted skin testing programs should only be conducted among high-risk groups.

http://www.cdc.gov/tb/publications/factsheets/testing/skintesting.htm
Blood Tests for TB Infection

- Interferon Gamma Release Assays (IGRA)
- Developed in 2001
- Measures the interferon gamma (IFN-γ) released in response to *M. tuberculosis* antigens

IGRAs:

**PROS:**
- Requires single patient visit
  “One and done”
- Results can be available within 24 hours
- Does not boost responses measured by subsequent tests
- Prior BCG vaccination does not cause a false-positive result
- Largely unaffected by most environmental nontuberculous mycobacteria (NTM)
- Data suggest not affected by intravesicular BCG

**CONS:**
- Expensive
- Blood samples must be processed 8-30 hours after collection
- Errors in collecting or transporting blood specimens or in running and interpreting the assay can decrease accuracy
- Inconsistent test reproducibility
- Limited data on effect of IGRA-guided therapy on prevention of TB disease
- False positive can occur in individuals infected with: *M. marinum, M. kansasii*
- May be boosted by TST (>3 days to 3 months)

**FDA-Approved IGRAS:** T-Spot, Quantiferon-TB Gold, Quantiferon-TB Gold Plus
IGRA Performance in Diagnosing LTBI in HIV+ Patients

- IGRAs (particularly TSPOT) may be more sensitive than TST in HIV-affected individuals and less affected by advanced immunosuppression

- IGRAs perform similarly to the TST in identifying HIV+ individuals who could benefit from LTBI therapy

- Low TB screening completion rates with TST may be improved by using IGRA

Cattamanchi et al. J Acquir Immune Defic Syndr 2011;56:230-238
IGRA vs. TST in HIV

- No definitive comparisons of tests for LTBI screening in persons with HIV in low-burden TB settings
- Use one or the other, not both
LTBI testing of ANY kind is preferable to NO TESTING
Evaluation of LTBI in HIV

- Assess for symptoms: fever, night sweats, weight loss, cough of any duration, lymphadenopathy
- CXR
- Assess for extrapulmonary TB:
  - more common in HIV
  - more common when CD4<200
Who to treat?

- A positive diagnostic test for LTBI and no prior history of treatment for active or latent TB

- A negative diagnostic test for LTBI but close contacts of persons with infectious pulmonary TB
Treating LTBI (to prevent TB disease)

Indications:
- (+) screening test* for LTBI, no evidence of active TB, and no prior history of treatment for active or latent TB (AI);
- Close contact with a person with infectious TB, regardless of screening test result (AII)

Preferred Therapy (Duration of Therapy = 9 Months):
- INH 300 mg PO daily + pyridoxine 25-50 mg PO daily (AII) or
- INH 900 mg PO twice weekly (by DOT) + pyridoxine 25-50 mg PO daily (BII)

Alternative Therapies:
- RIF 600 mg PO daily x 4 months (BIII) or
- RFB (dose adjusted based on concomitant ART) x 4 months (BIII) or
- RPT (weight-based, 900 mg max) PO weekly + INH 15 mg/kg weekly (900 mg max) + pyridoxine 50 mg weekly x 12 weeks – in patients receiving an EFV- or RAL-based ART regimen (BIII)
  - 32.1–49.9 kg 750 mg
  - ≥50.0 kg 900 mg
- For persons exposed to drug-resistant TB, select anti-TB drugs after consultation with experts or with public health authorities (AII)

*Treatment of LTBI decreases the risk of TB disease in HIV-positive individuals by 62%, risk of death by 26%  
*Protective effect of LTBI treatment is durable

https://aidsinfo.nih.gov/guidelines
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- I arrived recently from another country where TB is common.
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- I was in close contact with someone with active TB disease.
- I have diabetes, kidney failure, or cancer.
- I had surgery to remove part of my stomach.
- I live or work in a hospital, jail, drug rehab center or shelter.
- I use injection drugs.
- I have received an organ transplant.
- I take certain medications that affect my immune system, like prednisone (steroids) or other pills or injections to treat certain types of skin, joint and gastrointestinal conditions.

If I have Latent TB Infection, can I reduce my chances of getting sick with Active TB Disease?

Yes, I can prevent tuberculosis!

I can take safe, effective medicines.
Diagnosis of Active TB in HIV

- Presentation of disease influenced by degree of immunodeficiency
- In HIV+ without pronounced immunodeficiency (CD4>350), TB clinically resembles disease seen in HIV-negative → pulmonary disease with typical x-ray
- Lower CD4 counts → atypical presentation of disease
- Extrapulmonary TB is also more common in HIV regardless of CD4 count:
  - disseminated/miliary disease
  - meningitis
  - lymphadenitis
- High level of suspicion necessary
Diagnosis of Pulmonary TB in HIV

- Most HIV-infected patients with pulmonary TB have symptoms: fever, cough, weight loss, night sweats
- Duration of symptoms is shorter in HIV-infected patients
- 25% of HIV+ individuals with pulmonary TB will have negative TST or IGRA
- CXR atypical or even normal with CD4 <200

• “Atypical” CXR findings include: lower lobe, middle lobe, interstitial or miliary infiltrates

http://www.searo.who.int/EN/Section10/Section18/Section356/Section421_1626.htm
Diagnosis of Pulmonary TB in HIV

- Obtain CXR
- AFB sputum smear x 3
- Nucleic-acid amplification testing: GeneXpert MTB/RIF, GeneXpert MTB/RIF Ultra
- Sputum for AFB culture and drug susceptibility
Treating Active TB Disease

- After collecting specimen for culture and molecular diagnostic tests, empiric treatment should be initiated in HIV-infected persons with clinical and radiographic presentation suggestive of HIV-related TB (AIII).
- DOT is recommended for all patients requiring treatment for HIV-related TB (AI).
- Please refer to the table below for TB drug dosing recommendations and to the Adult and Adolescent ARV Guidelines for dosing recommendations of ARV drugs when used with RIF or RFB.

For Drug-Sensitive TB

**Intensive Phase (2 Months)**
- INH + (RIF or RFB) + PZA + EMB (AI); if drug susceptibility report shows sensitivity to INH & RIF, then EMB may be discontinued.

**Continuation Phase (For Drug-Susceptible TB)**
- INH + (RIF or RFB) daily (5–7 days per week) (AII)

**Total Duration of Therapy:**
- Pulmonary, drug-susceptible TB—6 months (BII)
- Pulmonary TB & positive culture at 2 months of TB treatment—9 months (BII)
- Extrapulmonary TB w/CNS involvement—9 to 12 months (BII)
- Extrapulmonary TB w/bone or joint involvement—6 to 9 months (BII)
- Extrapulmonary TB in other sites—6 months (BII)

**For Drug-Resistant TB**

**Empiric Therapy for Suspected Resistance to Rifamycin +/- Resistance to Other Drugs:**
- INH + (RIF or RFB) + PZA + EMB + (moxifloxacin or levofloxacin) + (an aminoglycoside or capreomycin)
- Therapy should be modified based on drug susceptibility results
- A TB expert should be consulted

**Resistant to INH**
- (RIF or RFB) + EMB + PZA + (moxifloxacin or levofloxacin) for 2 months (BIII); followed by (RIF or RFB) + EMB + (moxifloxacin or levofloxacin) for 7 months (BII)

**Resistant to Rifamycins +/- Other Antimycobacterial Agents:**
- Therapy and duration of treatment should be individualized based on drug susceptibility, clinical and microbiological responses, and with close consultation with experienced specialists (AIII).
Daily Therapy

- TB regimens that included twice- or thrice-weekly dosing during the initial intensive phase of therapy have been associated with an increased risk of treatment failure or relapse with acquired rifampin resistance.
- Daily therapy is recommended over the entire course of therapy via directly-observed therapy (DOT).
Video Directly Observed Therapy

- The use of remote video by a healthcare provider to observe a patient ingesting medications
- North Carolina: in person DOT for at least first two weeks, uses Facetime, Skype
- Georgia: in person DOT for first 8 weeks, uses Skype

Timing of ART in TB/HIV Disease

- Concurrent therapy is challenging due to:
  - High pill burden
  - Increased potential drug toxicity
  - Increased risk of drug interactions
  - Risk of TB-associated IRIS

- Delaying HAART until after completion of TB therapy increases AIDS-associated morbidity and mortality
Timing of ART in TB/HIV Disease

- CD4<50: start ART within two weeks of starting TB therapy
- CD4 ≥50: ART should be started within 8 weeks of starting TB therapy
- When TB occurs in patients already on ART, start TB medications immediately and choose rifamycin that does not lead to drug interactions with ART

**early ART not necessarily beneficial in TB meningitis**
Table 5. Drug-drug Interactions with Rifamycins and ART


<table>
<thead>
<tr>
<th>Rifampin (RIF)(^{17})-based Regimen with ART</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>NUCLEOSIDE REVERSE TRANSCRIPTASE INHIBITORS (NRTIs)</strong></td>
</tr>
<tr>
<td>Do not use RIF with tenofovir alafenamide (TAF) containing regimens (i.e. Biktarvy(^{®}), Descovy(^{®}), Genvoya(^{®}), Odefsey(^{®}))</td>
</tr>
<tr>
<td><strong>NON-NUCLEOSIDE REVERSE TRANSCRIPTASE INHIBITORS (NNRTIs)</strong></td>
</tr>
<tr>
<td>Efavirenz (EFV) 600 mg po every night (standard). Consider TDM.</td>
</tr>
<tr>
<td>Do not use RIF with etravirine (ETR), nevirapine (NVP), or rilpivirine (RPV).</td>
</tr>
<tr>
<td><strong>PROTEASE INHIBITORS (PIs)</strong></td>
</tr>
<tr>
<td>Do not use RIF with any PI (boosted or unboosted) containing regimen.</td>
</tr>
<tr>
<td><strong>INTEGRASE STRAND TRANSFER INHIBITORS (INSTIs)</strong></td>
</tr>
<tr>
<td>Increase dolutegravir (DTG) to 50 mg po bid. Use alternative to RIF if INSTI-experienced with certain INSTI-associated resistance substitutions or clinically suspected INSTI resistance.</td>
</tr>
<tr>
<td>Increase raltegravir (RAL) to 800 mg po bid. Do not use once daily RAL with rifampin.</td>
</tr>
<tr>
<td>Do not combine RIF with bictegravir/emtricitabine/TAF (Biktarvy(^{®}))</td>
</tr>
<tr>
<td>Do not use RIF with elvitegravir (EVG) containing regimens (i.e., Genvoya(^{®}) or Stribild(^{®}))</td>
</tr>
<tr>
<td><strong>CCR5 INHIBITOR</strong></td>
</tr>
<tr>
<td>Use MVC 600 mg bid with RIF, or 300 mg bid if used with RIF and a strong CYP3A inhibitor</td>
</tr>
<tr>
<td>NRTIs</td>
</tr>
<tr>
<td>------</td>
</tr>
<tr>
<td>Do not use RFB with TAF containing regimens (i.e. Biktarvy®, Descovy®, Genvoya®, Odefsey®)</td>
</tr>
</tbody>
</table>

| NNRTI | 
|------|---|
| EFV (standard dose) | RFB 450–600 mg/day; or RFB 600 mg 3 times/week if EFV is not coadministered with a PI |
| ETR (standard dose) | RFB 300 mg po once daily (standard dose). Do not combine ETR with RFB if used with a RTV-boosted PI. |
| NVP (standard dose) | RFB 300 mg po once daily (standard dose) |
| RPV | Increase RPV to 50 mg po once daily. |

| PIs | 
|------|---|
| Ritonavir (/r) or Cobicistat (/c)-boosted PIs[^18] | 
| Atazanavir (ATV)/r or ATV/c | RFB 150 mg po once daily |
| Darunavir (DRV)/r or DRV/c | Monitor for antimycobacterial efficacy, adverse effects, and consider TDM |
| Lopinavir/r | 
| Tipranavir/r | 

| Unboosted PIs | 
|------|---|
| ATV | RFB 150 mg po once daily |

| INSTIs | 
|------|---|
| No dosage adjustments for DTG or RFB[^18] | 
| No dosage adjustments for RAL or RFB[^19] | 
| Do not combine RFB with bictegravir/emtricitabine/TAF (Biktarvy®) | 
| Do not combine RFB with elvitegravir/cobicistat/emtricitabine/tenofovir (Stribild® or Genvoya®). | 

| CCR5 INHIBITOR | 
|------|---|
| MVC 150 mg po bid (with potent CYP3A inhibitor); MVC 300 mg po bid (without potent CYP3A inhibitor or inducer); Dose RFB based on other drugs in regimen (consider TDM) |
Adverse Drug Reactions in TB Patients on ART

- TB medications and antiretrovirals share similar adverse drug reactions:
  - drug-induced liver injury
  - rash
- Due to multiple medications, it may be difficult to determine cause
TB-IRIS

- Relatively common in patients starting ART while on TB treatment (8%-43%)
- Risk factors: CD4<100, extrapulmonary or disseminated TB, short interval between starting TB meds and ART, high viral load
- Symptoms typically occur 1-4 weeks after ART initiated

ATS/CDC/IDSA Clinical Practice Guidelines for Drug-Susceptible TB. CID 2016:63 (1 October)
TB-IRIS

- Patients usually improve on TB therapy, then develop new or recurrent symptoms within the first few weeks of ART
- Common manifestations:
  - fevers
  - new or worsening lymphadenopathy
  - new or worsening respiratory symptoms
  - new or worsening radiographic findings
- Diagnosis based on: clinical presentation with typical timeline, demonstration of response to ART (↑CD4, ↓VL), r/o alternative causes for deterioration like: treatment failure from drug resistant TB, other OIs

ATS/CDC/IDSA Clinical Practice Guidelines for Drug-Susceptible TB. CID 2016:63 (1 October)
TB-IRIS

Treatment:
- symptomatic; treat with anti-inflammatorie
- most cases self-limiting
- steroids used in cases with significant symptoms: prednisone 1.25 mg/kg/day for 2-4 weeks with tapering over a period of 6-12 weeks or longer

ATS/CDC/IDSA Clinical Practice Guidelines for Drug-Susceptible TB. CID 2016:63 (1 October)
TB/HIV Pearls

- Early diagnosis and treatment of HIV will help reduce TB risk
- Early assessment for latent TB infection and treatment (if indicated)
- Educate patients and providers on signs and symptoms of TB
TB/HIV Pearls

- When treating active TB, work closely with TB Control nurses, case managers, outreach workers
- Give TB/HIV medications together when able
- After completion of TB therapy, ensure continuation of HIV care and maintained virologic suppression
- Thank you!
<table>
<thead>
<tr>
<th>Activity</th>
<th>Baseline</th>
<th>Month of Treatment Completed</th>
<th>End of Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Microbiology</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Sputum smears and culture(^6)</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Drug susceptibility testing(^7)</td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Imaging</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CXR or other imaging(^8)</td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Clinical Assessment</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Weight(^9)</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Symptom and adherence review(^10)</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Vision assessment(^11)</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Laboratory Testing</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>AST, ALT, bilirubin, alkaline phosphatase(^12)</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Platelet count(^13)</td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Creatinine(^13)</td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HIV testing(^14)</td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hepatitis B and C screen(^15)</td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diabetes Screen(^16)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
US TB Cases, 2017: 9093

- Florida, 549
- Georgia, 290
- Tennessee, 128
- North Carolina, 213
- South Carolina, 181
- Kentucky, 65
- Mississippi, 53
- Alabama, 120

Tuberculosis—United States, 2017. MMWR 2018;76:[317-323]
The Online TST/IGRA Interpreter

Version 3.0

The following tool estimates the risk of active tuberculosis for an individual with a tuberculin skin test reaction of ≥5mm, based on his/her clinical profile. It is intended for adults tested with standard tuberculin (5 TU PPDS, or 2 TU RT-23) and/or a commercial Interferon Gamma release assay (IGRA). For more details about the algorithm used, go to the About page. The current version of the algorithm contains modifications of the original version, which was detailed in a paper by Menzies, et al (2008). For further information see references, or contact dick.menzies@mcgill.ca

Please select the best response for each field:

TST Size:  
Select...  

IGRA Result:  
IGRA Not Done  

Age:  
Select...  

N/A  

Age at immigration (if person immigrated to a low TB incidence country):

Country of birth:  
Select...  

BCG status:  
Select...  

For more info, visit: BCG World Atlas.

Recent contact with active TB:  No Contact  

Please select all the conditions that currently apply to the patient:  
(If none of these conditions apply, please leave boxes unchecked)

- AIDS
- Abnormal chest x-ray: fibronodular disease
- Chronic renal failure requiring hemodialysis
- Diabetes Mellitus (all types)
- HIV infection
- Abnormal chest x-ray: granuloma
- Carcinoma of head and neck
- Cigarette smoker (>1 pack/day)
### Groups with Increased Likelihood of Infection with Mtb

<table>
<thead>
<tr>
<th>Risk of Infection</th>
<th>Benefit of Therapy</th>
<th>LTBI Testing Strategy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Household contact or recent exposure of an active case</td>
<td>Yes</td>
<td>Likely to be Infected Low to Intermediate Risk of Progression (TST ≥ 10mM)</td>
</tr>
<tr>
<td>Mycobacteriology laboratory personnel</td>
<td>Not demonstrated</td>
<td>Likely to be Infected High Risk of Progression (TST ≥ 5mM)</td>
</tr>
<tr>
<td>Immigrants from high burden countries (&gt;20 / 100,000)</td>
<td>Not demonstrated</td>
<td></td>
</tr>
<tr>
<td>Residents and employees of high risk congregate settings</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>Not demonstrated</td>
<td>Unlikely to be Infected (TST &gt; 15mM)</td>
</tr>
</tbody>
</table>

### Risk of Developing Tuberculosis if Infected

<table>
<thead>
<tr>
<th>Risk of Developing Tuberculosis if Infected</th>
<th>Low</th>
<th>Intermediate (RR 1.3 -3)</th>
<th>High (RR 3-10)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No risk factors</td>
<td>Clinical predisposition</td>
<td>Children age less than 5</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Diabetes</td>
<td>HIV infection</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Chronic renal failure</td>
<td>Immunosuppressive therapy</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Intravenous drug use</td>
<td>Abnormal CXR consistent with prior TB</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Silicosis</td>
<td></td>
</tr>
</tbody>
</table>

### Benefit of Therapy

<table>
<thead>
<tr>
<th>Benefit of Therapy</th>
<th>Not demonstrated</th>
<th>Yes</th>
</tr>
</thead>
</table>

In developing a diagnostic approach for the evaluation of those with suspected LTBI, we recommend the clinician weigh the likelihood of infection, the likelihood of progression to TB if infected, and the benefit of therapy (Horsburgh, C.R., Jr., and E.J. Rubin. 2011. Clinical practice. Latent tuberculosis infection in the United States. The New England journal of medicine 364:1441-1448). Recommendations were formulated for each of the three groups illustrated above. These groups are concordant with current recommendations for the interpretation of the TST (2000. Targeted tuberculin testing and treatment of latent tuberculosis infection. American Thoracic Society: MHAAP Practice Ryan. 49.1-51).
Questions / Answers
Thank You